REMARKS

The Official Action of 19 July 2005 has been carefully considered and reconsideration of the application as amended is respectfully requested.

The claims have been amended to remove the bases for the rejections under 35 USC 112, second paragraph, appearing at paragraphs 8a-c of the Official Action. All claims as amended are respectfully believed to be sufficiently definite to satisfy the dictates of 35 USC 112, second paragraph.

Claims 16-18 and 23-32 stand rejected under 35 USC 103(a) as allegedly being unpatentable over Nodiff in view of Paliwal et al and Puri et al. Applicants respectfully traverse this rejection.

Each of the claims under rejection is directed to a method for inhibiting transmission of malaria by the administration of **a single dose** of the claimed compound to an animal. The invention defined by these claims is based upon Applicants' discovery that a single dose of the claimed compound within the recited amount has gametocytocidal activity. In particular, the experimentation described in the specification at pages 14-15 and Table I on page 18 shows that the claimed compound kills gametocytes of *P. cynomolgi* within erythrocytes in blood of Rhesus monkeys when the recited compound is administered in a single dose in any of the claimed amounts within a seven day period (see Table I on page 18 of the specification). The specification also shows that the monkeys were not infective even after the seven day period

shown in Table I (see specification at page 15, first full paragraph).

The Examiner has acknowledged that the cited art does **not** teach the recited dosage of the claimed compound (Official Action at page 3, second paragraph), but maintains that one of skill in the art would be motivated to combat malaria by replacing the toxic primaquine with the recited compound because it is less toxic, either as a single dose or daily. However, the Examiner has respectfully not provided any explanation as to why, in the absence of the hindsight provided by the present specification, one of skill in the art would have had even a reasonable expectation that a **single dose** of the **claimed compound** would have effective gametocidal activity.

To establish a *prima facie* case of obviousness, the USPTO has the burden of, among other things, showing that there is a reasonable expectation of success with the invention **as claimed** (see MPEP Section 706.02(j)). Thus, whether or not one of skill in the art would have used the recited dose regimen of **primaquine** to combat malaria is not the controlling question. The controlling question is whether one of skill in the art would have had a reasonable expectation of success in the claimed method with a single dose of the claimed compound. If (as noted by the Examiner at paragraph 6 of the Official Action in connection with the enablement rejection discussed below) "the high degree of unpredictability is well recognized in the pharmaceutical art", then how can it be said that there would have been a reasonable expectation of success with the claimed compound in the recited dosage when the prior art does not teach the effectiveness of the claimed compound at this dosage?

Applicants respectfully submit that there would have been no reasonable expectation of success in the use of the claimed compound to provide gametocytocidal activity by virtue of any alleged gametocytocidal activity of primaquine. Puri et al show that compound 80/53 and primaquine have different properties, and in particular that compound 80/53 has a lower toxicity than primaquine. Accordingly, and in view of the unpredictability in the art alleged by the Examiner, it is respectfully submitted that the gametocytocidal activity of the claimed compound could not have been predicted from any alleged gametocytocidal activity of primaquine such that the cited references do not provide even a reasonable expectation of success with the claimed method. For this reason, it is respectfully submitted that the references do not set forth even a *prima facie* case of obviousness and that the prior art rejection of record should be withdrawn.

Claims 11 and 24 and the claims depending therefrom stand rejected under 35 USC 112, first paragraph, for alleged violation of the written description requirement. With respect to the rejection of claim 24 and the claims depending therefrom, the amendment to the claim to remove the alleged indefiniteness under 35 USC 112, second paragraph (see discussion above) is respectfully believed to remove the basis for the rejection under 35 USC 112, first paragraph. In this connection, Applicants respectfully note that the Table on page 18, when read in conjunction with the specification at page 15, first full paragraph, makes clear that the recited single dose may reduce infectivity for seven or more days.

With respect to claim 11 and the claims depending therefrom, it is respectfully submitted

that the rejection is based upon the Examiner's assumption that "1.0mg/kg of compound 1" in Table IV is an error. However, Applicants respectfully submit that this is an unwarranted assumption and cannot be used to satisfy the USPTO burden of setting forth even a *prima facie* violation of the written description requirement (see MPEP Section 2163.04: "The examiner, therefore, must have a reasonable basis to challenge the adequacy of the written description. The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims."). In this respect, Applicants respectfully note that the curative dose referred to on page 16 is the **antirelapse** curative dosage (line 16), and this description does not, in any event, preclude a different dosage.

Claims 11-15 and 23 stand rejected under 35 USC 112, first paragraph, for alleged violation of the enablement requirement. Applicants respectfully traverse this rejection.

The rejection appears to be based upon the contention that the recited dosage of the claimed compound would not be sufficient to inhibit malaria transmission. First, Applicants respectfully note that the claim has been amended to include a dosage of 1.0 mg/kg of the body weight of the animal as described in Table IV on page 22 of the specification. Next, Applicants respectfully note that the curative dose referred to on page 16 of the specification is an antirelapse curative dose, and does not mean that a lesser dosage would be ineffective in inhibiting malaria transmission. This being the case, it is respectfully submitted that the Examiner has not carried the USPTO burden of setting forth a *prima facie* case of obviousness for the

invention as claimed (see MPEP Section 2164.04: "In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention.").

In view of the above, it is respectfully submitted that all rejections and objections of record have been overcome, and that the application is now in allowable form. An early notice of allowance is earnestly solicited and is believed to be fully warranted.

Respectfully submitted,

CLIFFORD J. MASS
LADAS & PARRY
26 WEST 61ST STREET
NEW YORK, NEW YORK 10023
REG. NO.30,086(212)708-1890